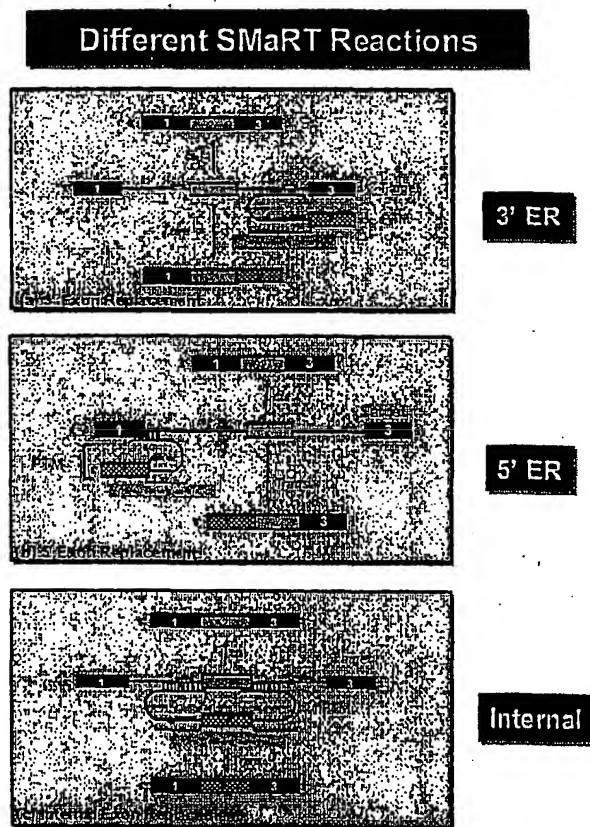


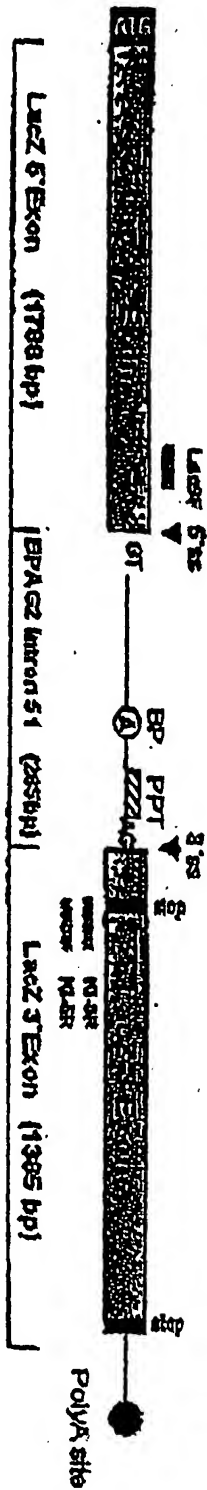
## FIGURE 1



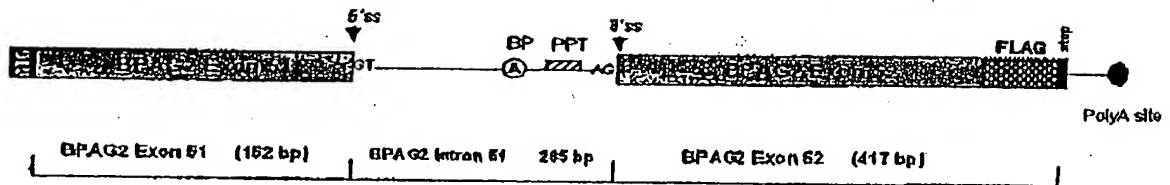
**Figure 1.** Schematic representation of different SMaRT reactions. (a) *Trans*-splicing reactions between the target 5' splice site and PTMs 3' splice site, (b) *Trans*-splicing reactions between the target 3' splice site and PTMs 5' splice site and (c) Replacement of internal exon by double *trans*-splicing reaction in which the PTM carry both 3' and 5' splice sites. BD, binding domain; BP, branchpoint sequence; PPT, polypyrimidine tract and ss, splice sites.

# FIGURE 2A

## 1) BPAG2 Target 1 (LacZ-T1)



**2) BPAG2 Target 2 (T2)**



**FIGURE 2B**

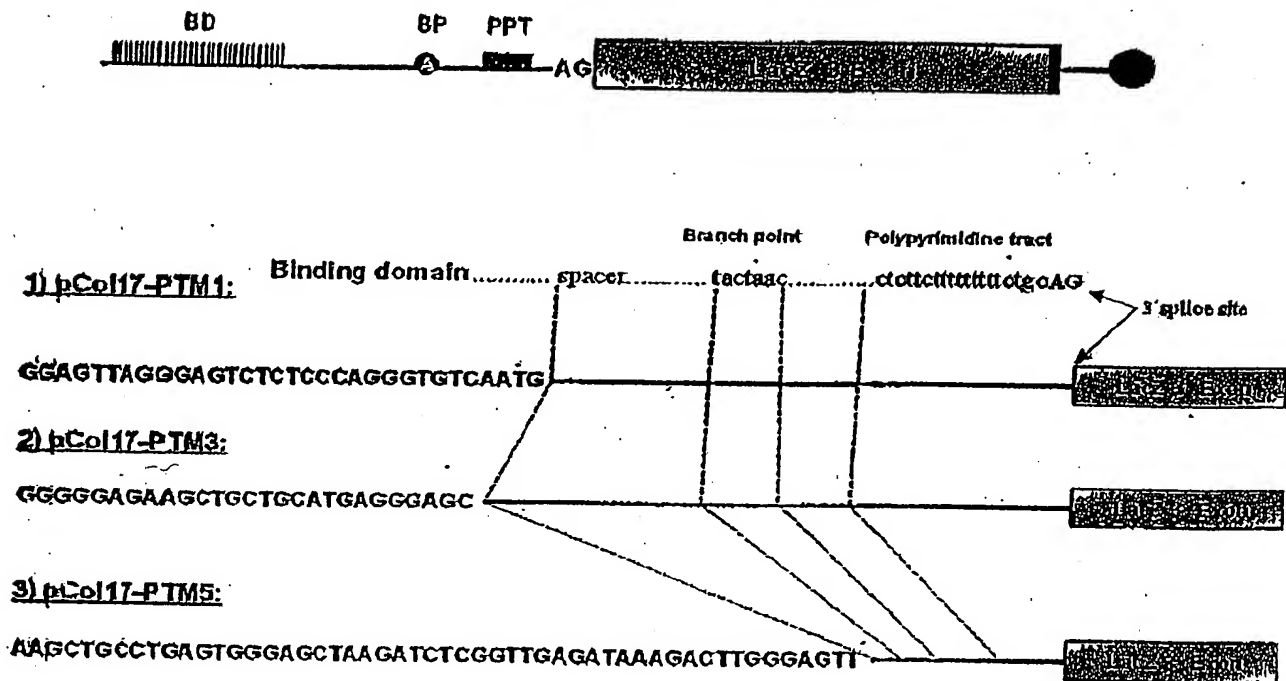
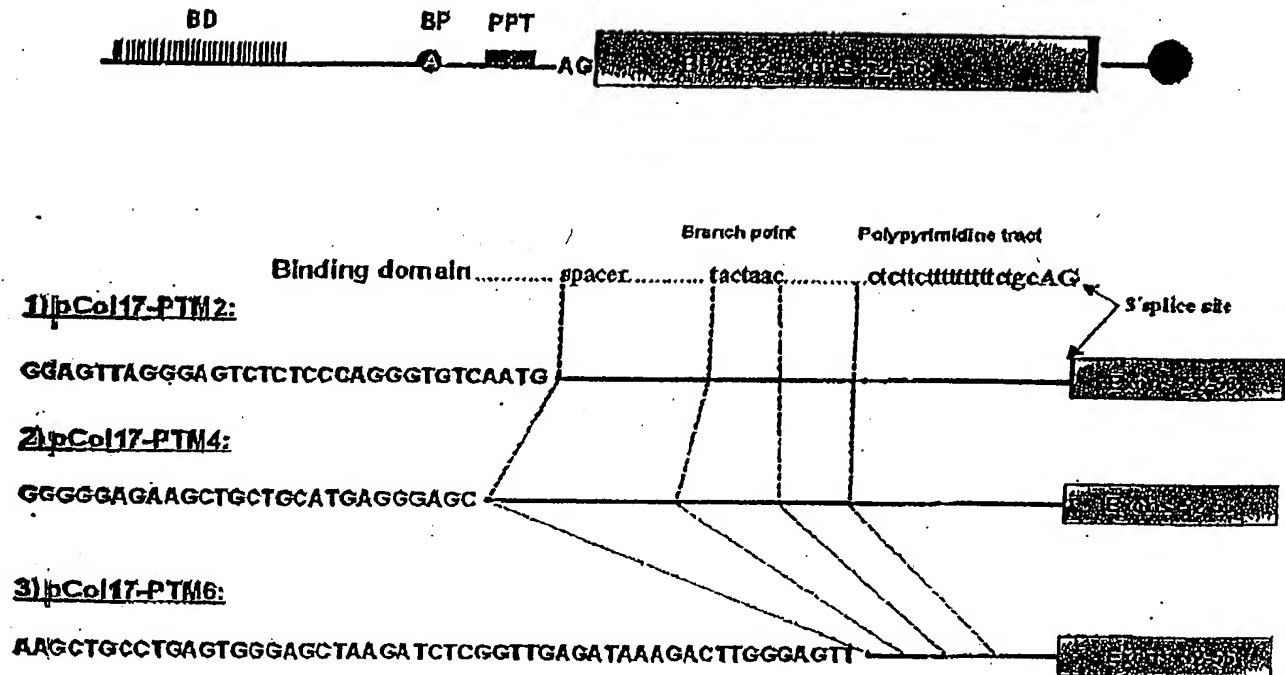
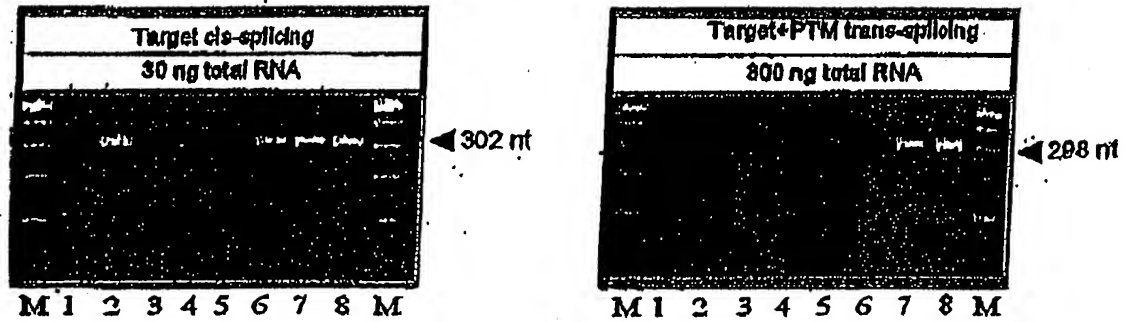


FIGURE 2C

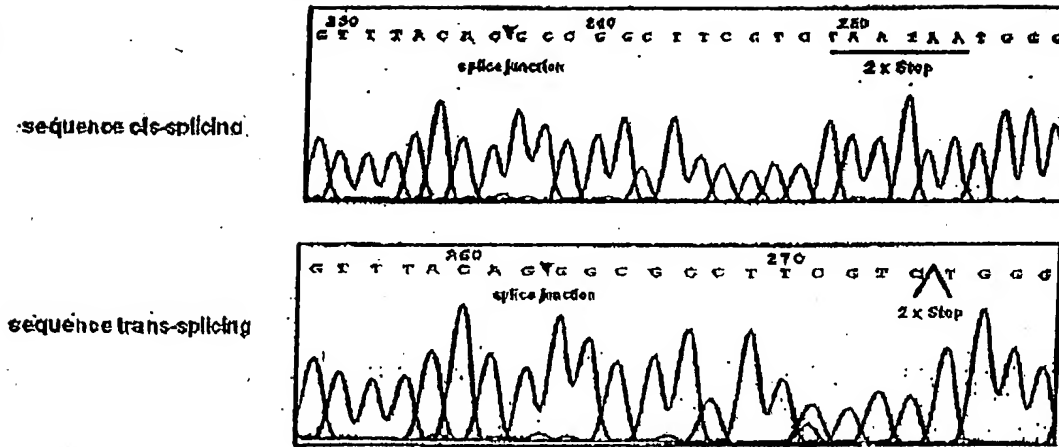


**FIGURE 2D**

**A**



**B**



**FIGURE 3A-B**

Q

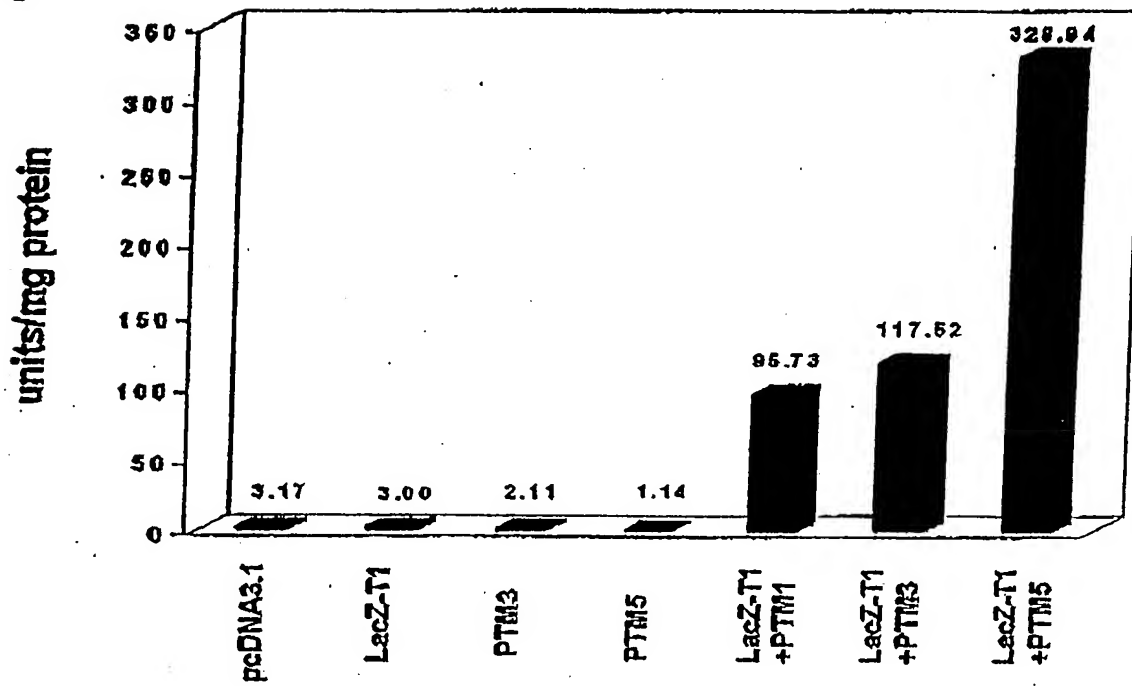
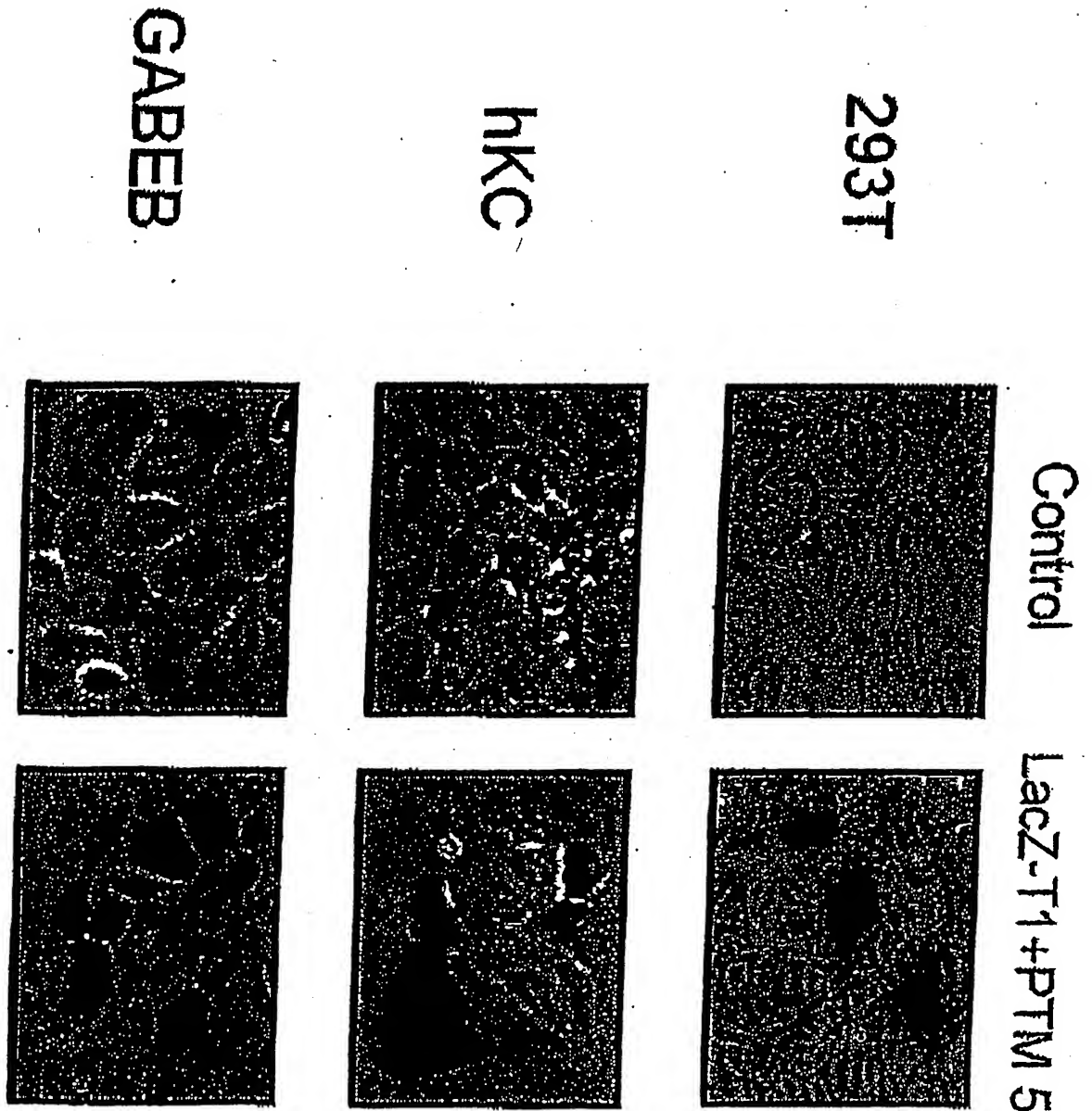


FIGURE 3C

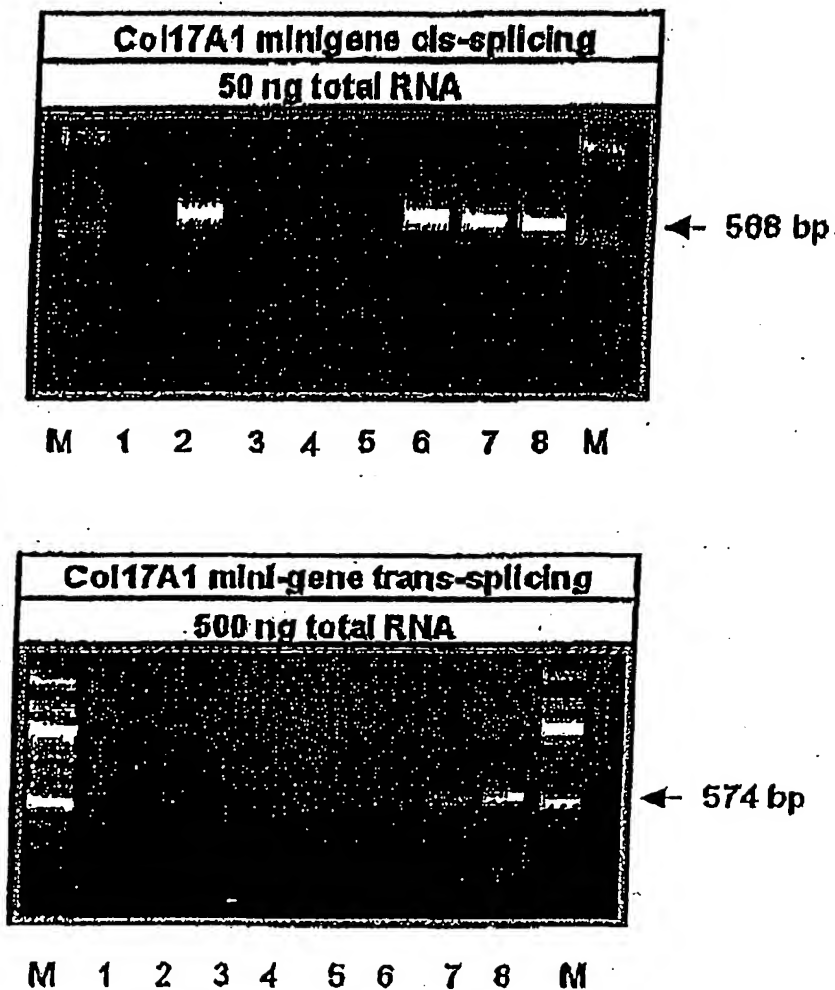


**FIGURE 4**

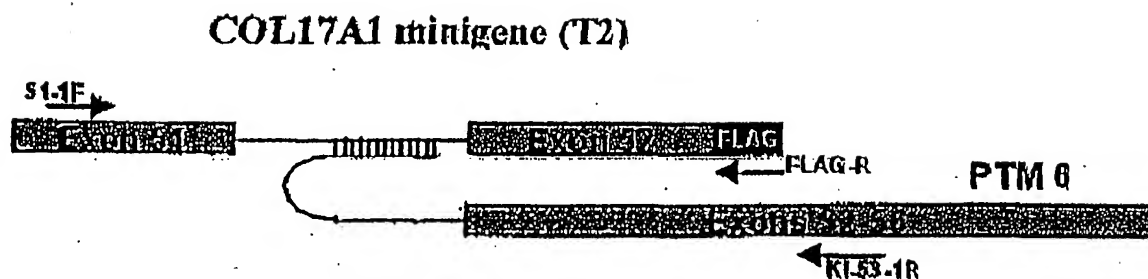


9/18

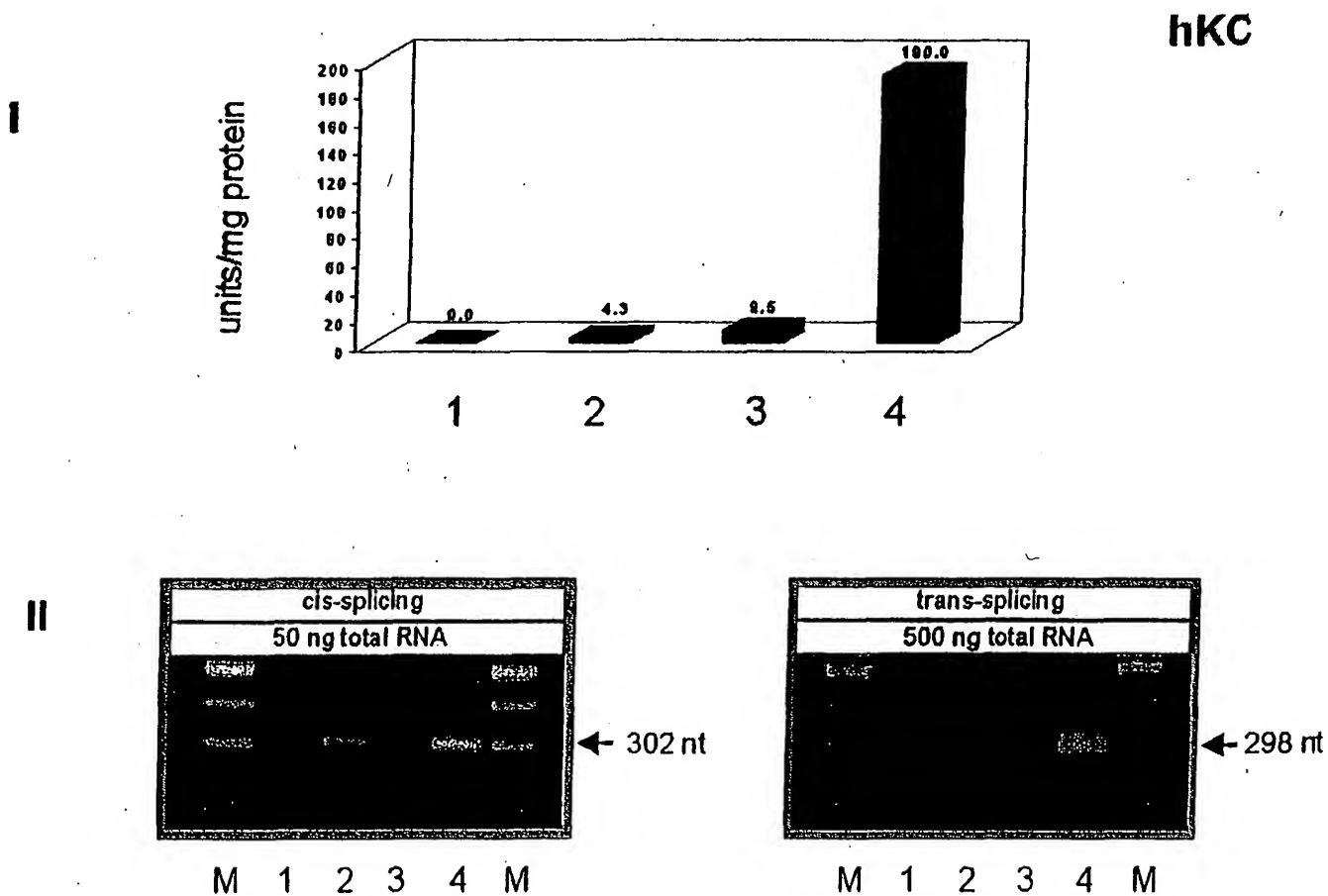
**A**



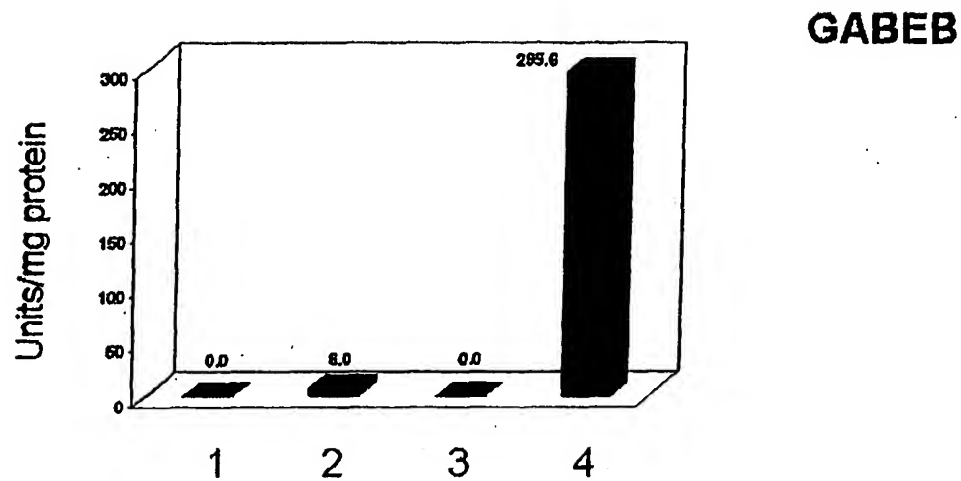
**B**



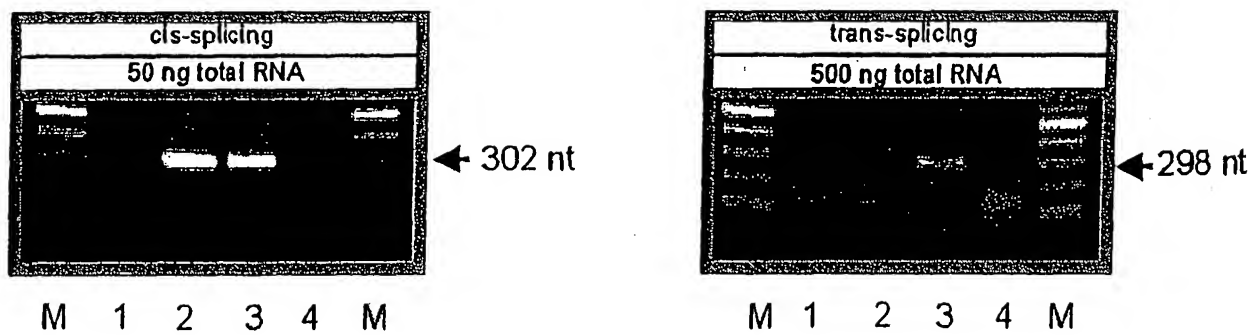
**FIGURE 5A-B**



**FIGURE 6A**



**II**



**FIGURE 6B**

# FIGURE 7

Detection Strategy for  
 Endogenous Trans-splicing in the  
 COL17A1 pre-mRNA in HecCatNC

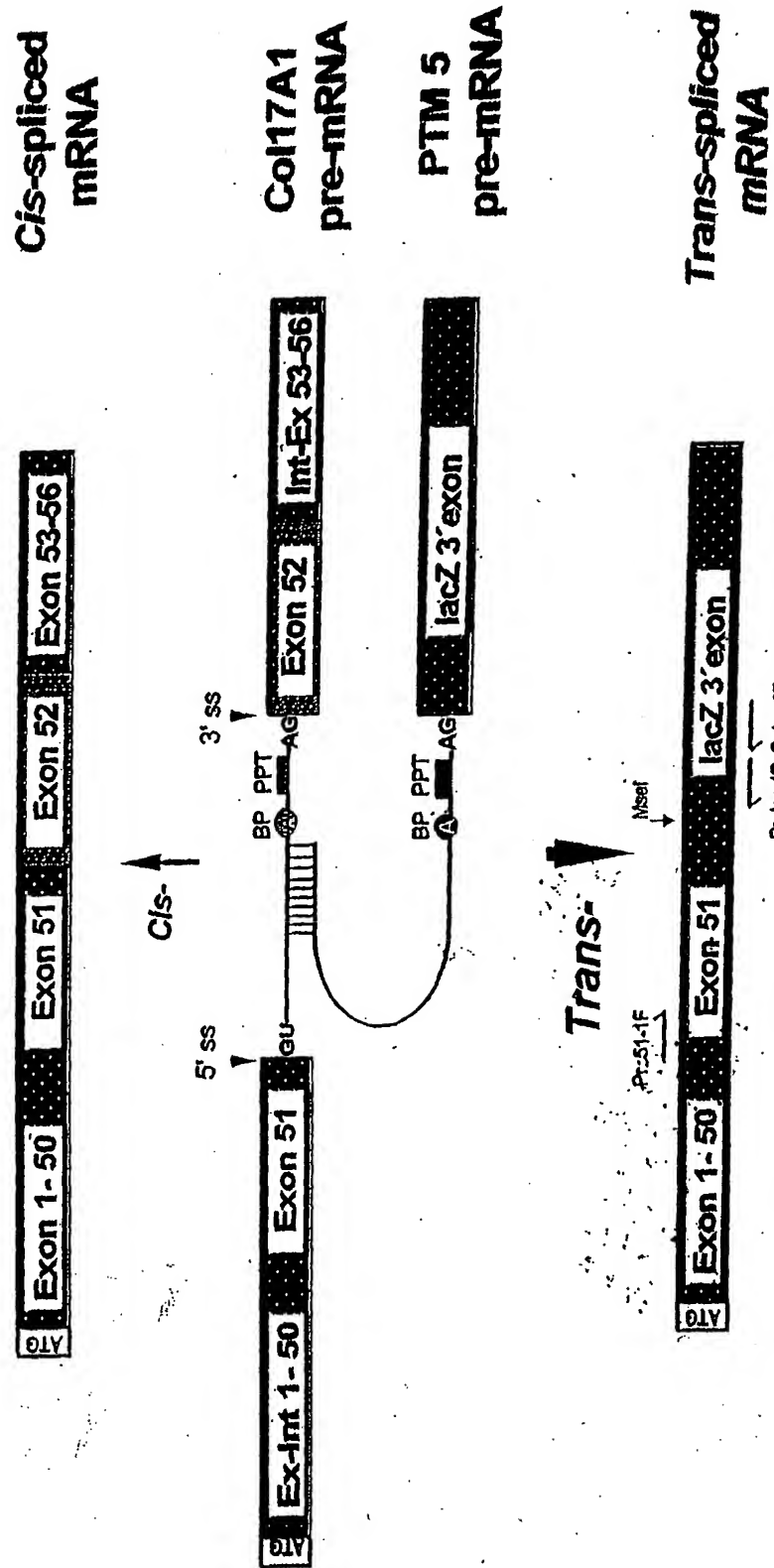
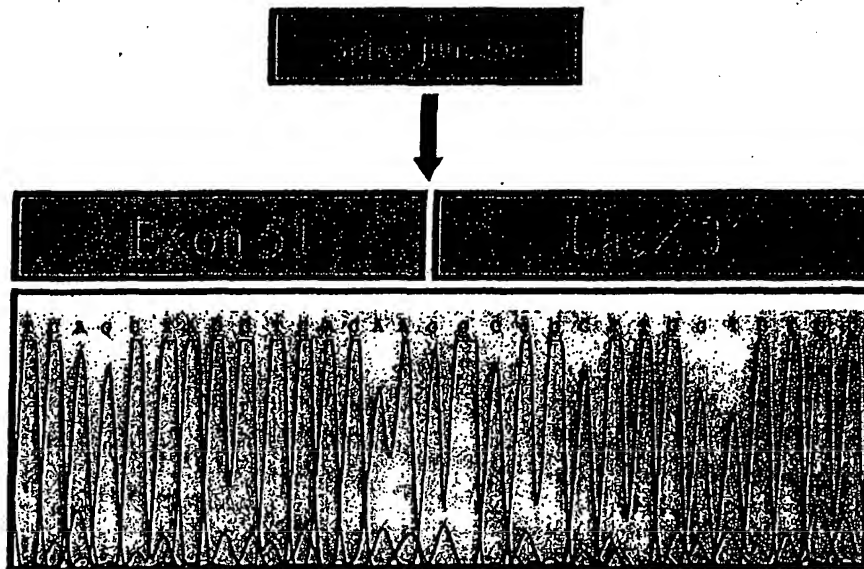


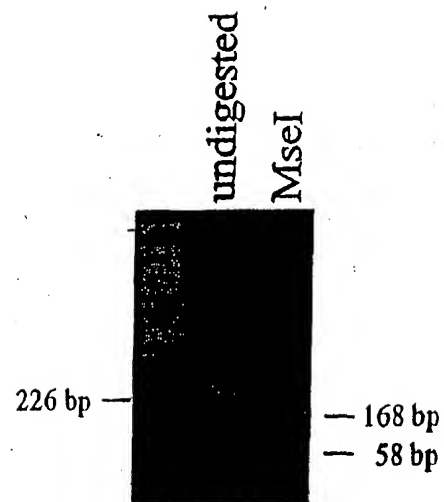
FIGURE 8

## Endogenous Transsplicing of Col17 pre-mRNA with PTM5 pre-mRNA

A)

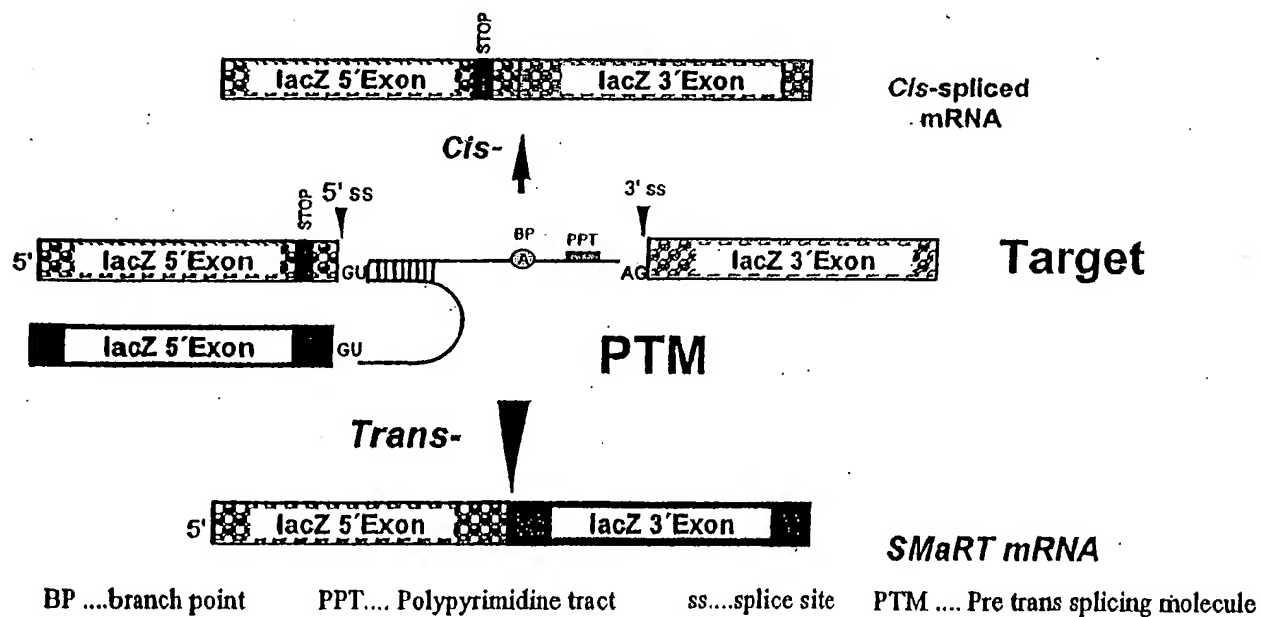


B)



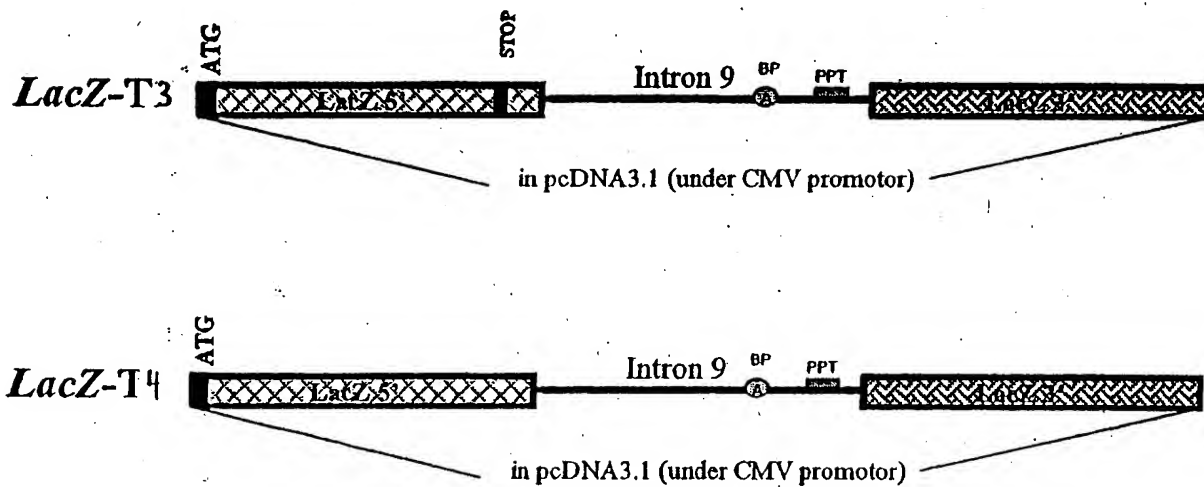
## FIGURE 9

### 5' trans-splicing in a LacZ-model system for hereditary diseases



## FIGURE 10

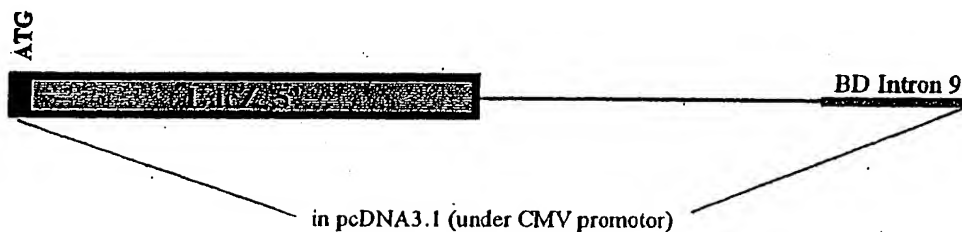
Target LacZ-T3 (containing Intron 9) and LacZ-T4 used for optimizing trans-splicing and transfection conditions



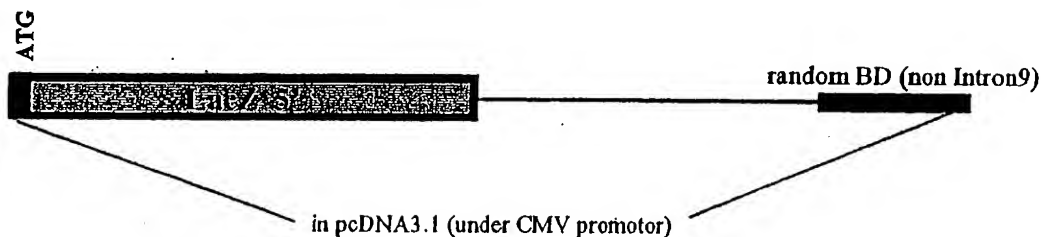
## FIGURE 11

LacZ-PTM-3 (Intron 9 specific binding domain) and LacZ-PTM-4 (non specific binding domain) for establishing optimal trans-splicing conditions

**Lac-PTM<sup>3</sup>**



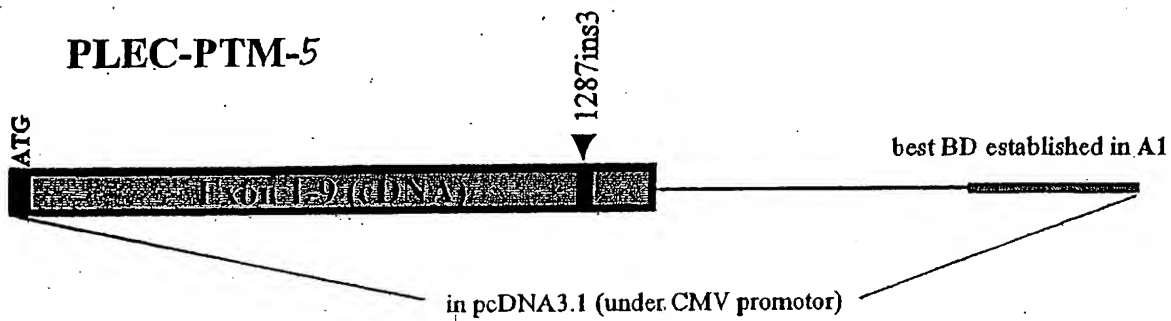
**Lac-PTM<sup>4</sup>**





## FIGURE 12

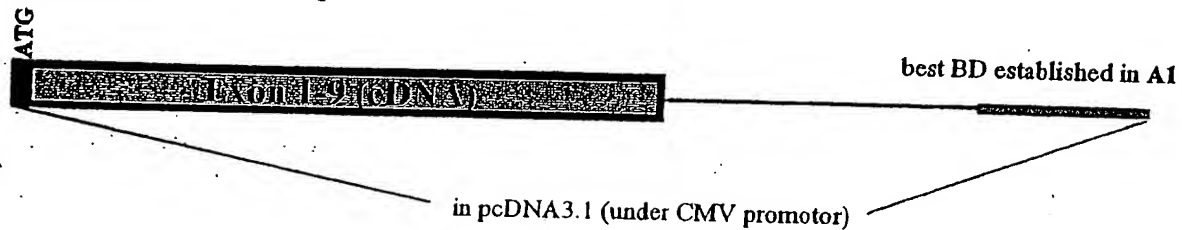
PLEC-PTM-5 for the introduction of the 1287ins3 mutation  
in 293T cells



## FIGURE 13

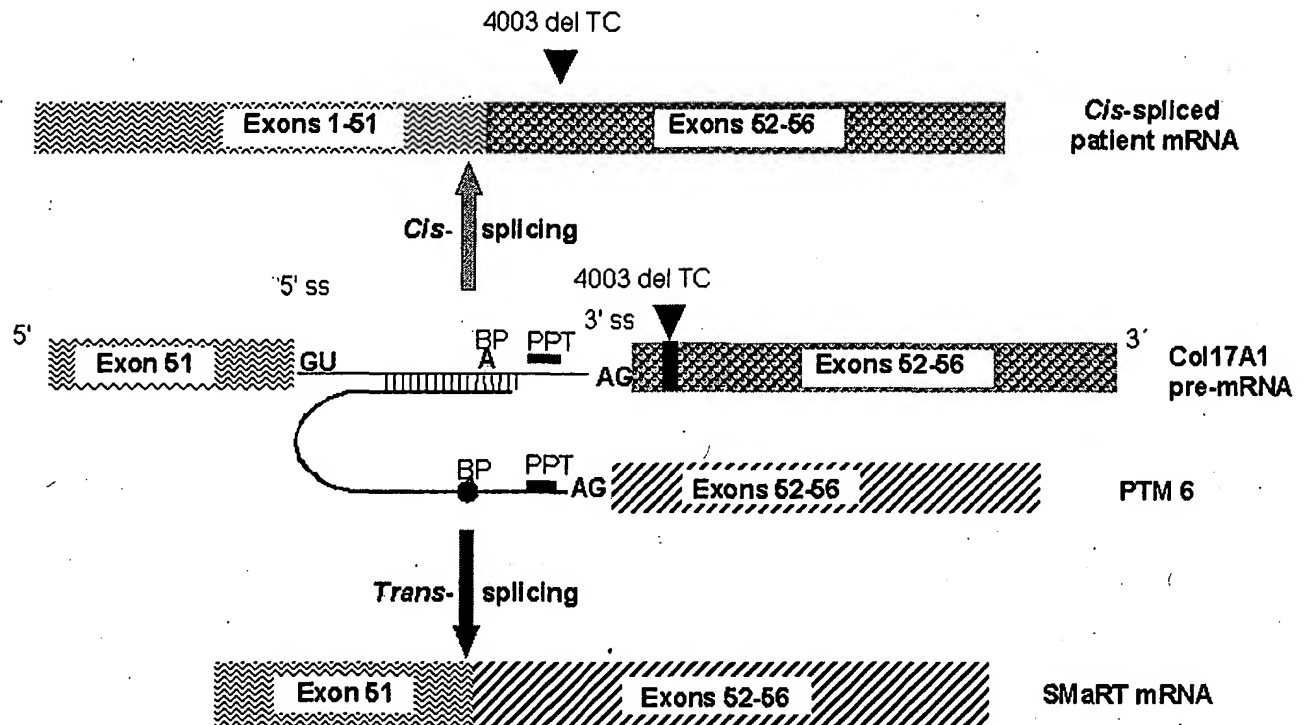
PLEC-PTM-6 for the repair of the 1287ins3 mutation  
in plectin deficient patient cells

PLEC-PTM-6



## FIGURE 14A

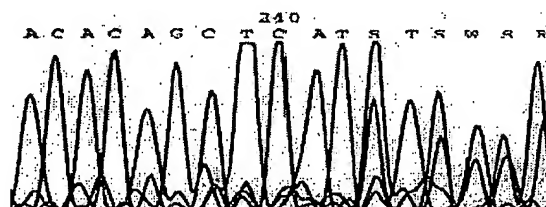
### **Trans-splicing Strategy for Col17A1 Gene (GABEB/generalized atrophic benign epidermolysis bullosa)**



## FIGURE 14B

# Semi-nested RT-PCR with BPAG2- primer 51-1F, 53-1R and 52-1R

RT-PCR

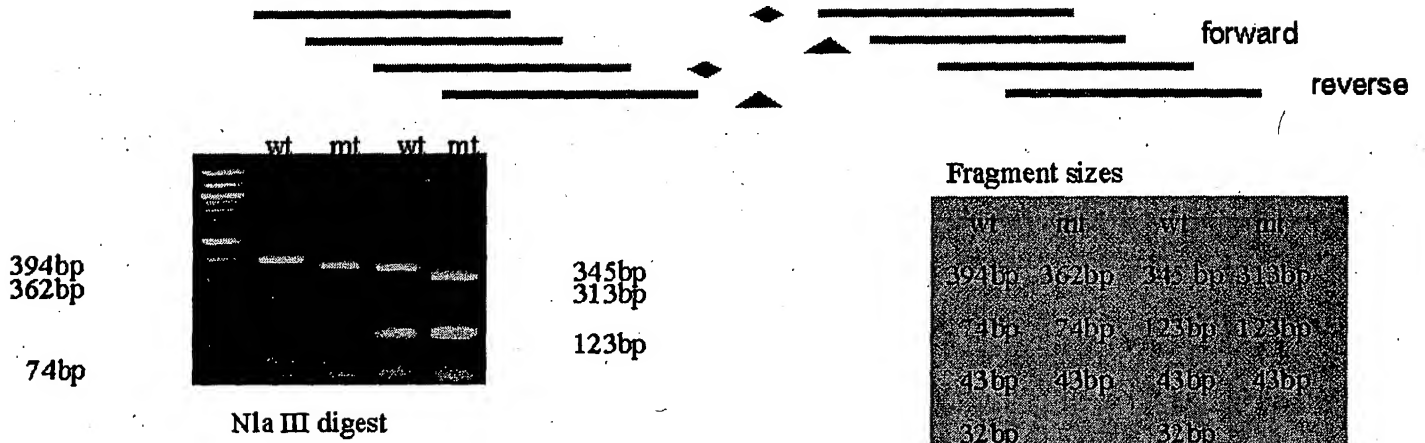


TCCTCTCA—M  
 TCTCAGC—M

F1  
 B1  
 C

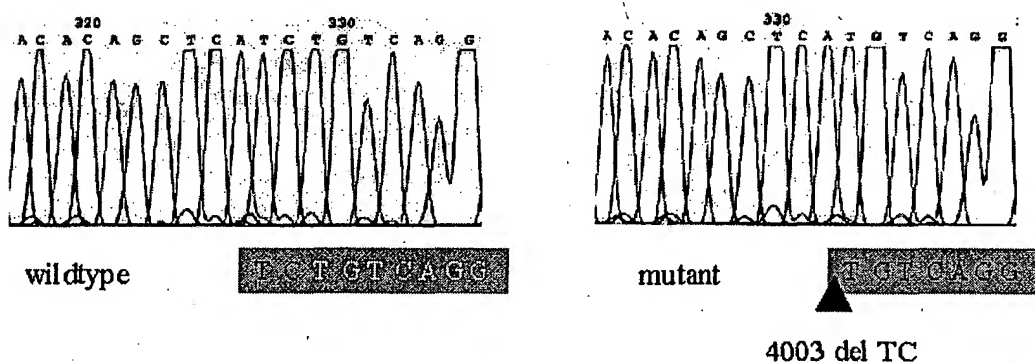
## FIGURE 14C

### TOPO Cloning + Nla III digest



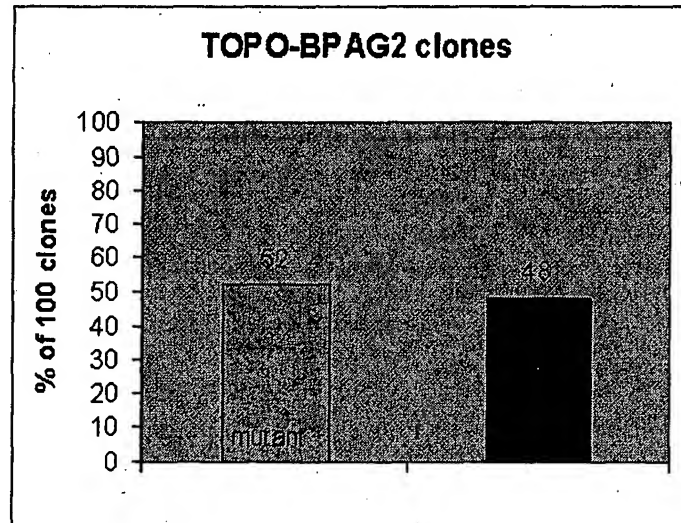
## FIGURE 14D

Sequencing of mutant and  
wildtype clones confirmed the  
correct *trans*-splicing of PTM6  
into GABEB cells



## FIGURE 14E

### Analysis of 100 clones



## FIGURE 15

# Immunofluorescence of PTM6- transfected GABEB cells

GABEB

non-transfected



GABEB

PTM6 transfected, 3 days

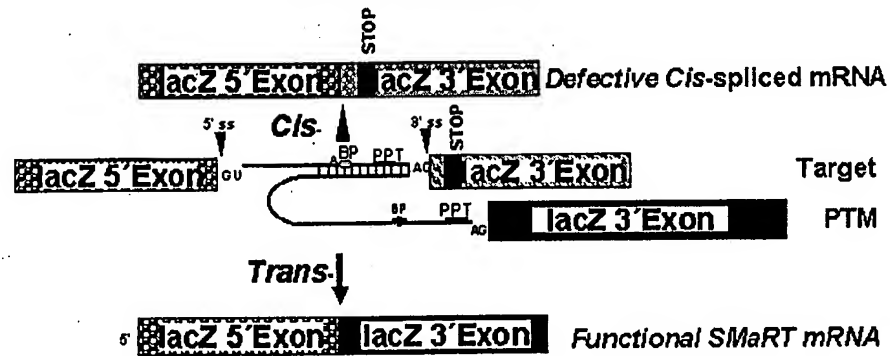




## FIGURE 16A-B

### *Trans*-splicing strategy for COL7A1 gene (Dystrophic epidermolysis bullosa)

A.



B.

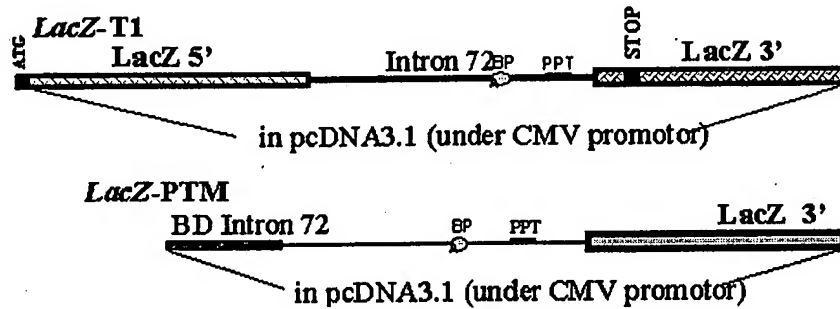
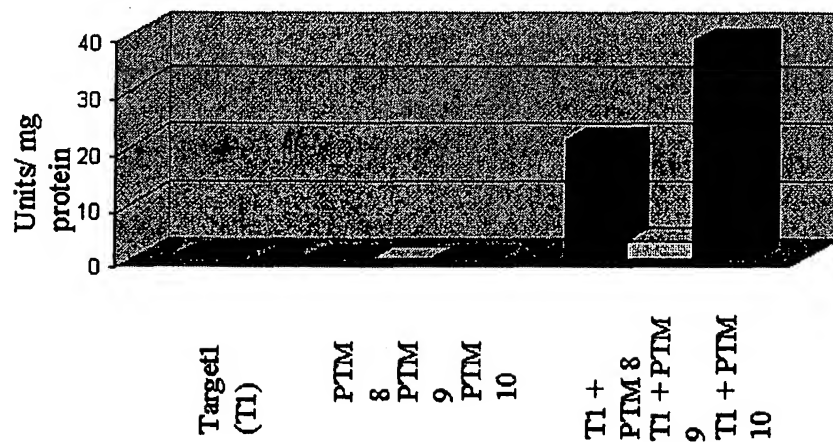


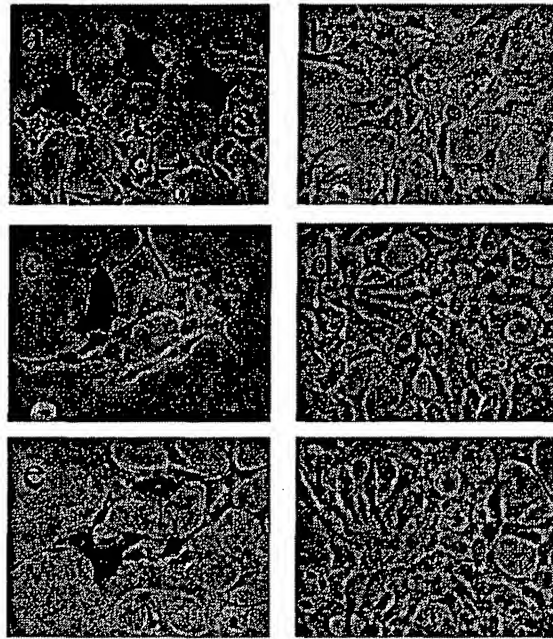
FIGURE 17

# $\beta$ -gal Assay of a Cotransfection of Col7 Target T1 and PTM 8, 9, 10 in 293T cells



## FIGURE 18

### Beta-gal staining of Col7 PTM transfected human 293T cells



left panel: (a) Target + PTM8, (c) Target + PTM9, (e) Target + PTM10;  
right panel: corresponding control PTM without Target.